IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	Dominic A. Cataldo, *et al.*
Serial No.	:	10/816,095
Filed:	:	April 1, 2004
For:	:	Use of Colloidal Clays for Sustained Release of Active Ingredients
TC/AU	:	1615
Examiner	:	Neil S. Levy
Attorney Docket No.	:	BGT 2-007

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DECLARATION UNDER RULE 131

Sir:

Declarant, Dominic A. Cataldo, does declare and state that:

1.   His professional credentials and work history are as set forth in his prior declarations, which are of record in the above-identified application;

2.   He has read the outstanding Office action mailed on February 19, 2009 and the Ohno citation.

3.   Ohno deals with a means to incorporate organic fungicides and inorganic anti-bacterial agents into a clay material which is chemically modified to alter the metal comprising the exchange sites within the clay to improve antifungal carrying capacity, water resistance, chemical resistance, prolonged antifungal/antibacterial activity, and weather resistance. This is accomplished by substitution one native (ion exchangeable) clay ions with Ca, H and/or F ions; for inorganic actives, toxic actives are incorporated into clay exchange sites. The goal is to create a carrier system suitable for incorporation into thermoplastic delivery systems.

4.   The Ohno approach for liquid organic actives is to mix inorganically modified clay with anti-microbial actives, grinding to incorporate the active, and reduce the particle size; alternatively, the active can be blended in a suitable solvent, mixed into clay with stirring, dried, then pulverized to size. Preparation parameters can be varied from pH of 0.1 to 13 (incompatible with the prior ion exchange needs), stirred for 0.5 to 72 hours, and use temperatures from 40° to 120°C. The inorganic anti-bacterial agents are incorporated

into a range of carriers by simple and known ion exchange methods. The latter (inorganic actives) is of no interest nor importance to Applicants.

5. Examples in Ohno, evaluation descriptions, methods, and data tables are informative in that they clearly show that the clay/bioactive formulations, which are non-crosslinked composites (as opposed to thermoplastics or thermosets) rather than polymers, demonstrates efficacy results out to 7 days, with the relative importance of color change not defined, and no use of bioactive (concentration controls) to determine whether these systems have any significant value.

6. Ohno has no relevance to our disclosure and claims for a number of reasons.

7. First, the manipulations of the exchangeable ions in clays and related materials have been done for years for a range of practical commercial reasons. We use organically substituted clays, which are selected to allow for maximum intercalation of active (demonstrated in attached data set below); these organic versus inorganic substitutions are important to the organic to organic exchange site interactions, and most importantly to retard physical diffusion from the intercalated layers.

8. Second, Ohno is concerned with developing a method that allows the use of inorganically modified clay to improve antifungal carrying capacity, water resistance, chemical resistance, prolonged antifungal/antibacterial activity, weather resistance, and as stated, thermal stability in thermoplastic applications. Ohno has demonstrated only weather resistance (UV protection), and possible use in compressed composites devices on vinyl chloride/plasticizer, and for only a few days, not years.

9. Third, Ohno reports and describes a system employing inorganically modified clays, that may retard water soluble losses, and protect the intercalated actives from UV degradation for days, but does not in any way describe a system where an active can be intercalated into a highly efficient carrier (>40% loading) using organically modified nano-clay (1-10μm) to retard diffusion from the carrier, to a thermoplastic or thermoset polymer for secondary diffusion rate control, and that can be incorporated to high temperature fabrication process (120° to 320°C), without significant loss of active.

10. Fourth, Ohno's reference to increasing active loading into his clays by repeated wet/solvent loading (pieces 1-3) simply is not effective in the loading accomplished by our thermal loading to a friable mixture, as seen in the data set below.

11. Finally, the intent of our approach dictates a release rate that can be controlled for many years, not a few days; this requires that we control diffusion-based release both from the intercalated clay reservoir and the polymer carrier. This requirement simply cannot be met using Ohno's methodology and approach.

12. Theoretical loading processes and requirements in our disclosed system:

Mixing clay and pesticide to the melting point, or just heating to improve clay absorption is different from our approach for 2 reasons. First, mixing and heating together as in Ohno, especially if the actives are solid below about 20°C, results in most of the active crystallizing on the surface of the clay. This surface fraction, which is generally greater than the absorbed fraction, serves no purpose with respect to the sustained release that we have targeted (2 to >20 years) in our desired product applications. Second, for the extended performance longevities that we target, the active must be contained within the intercalated clay structure, and not on the outside. This allows both the physical entrainment and ionic associations of the active within the clay structure to limit the amount of active entering the heated polymer (120° to 350°C) to be minimized during production, and maximizing the amount of active remaining intercalated within the clay. It is this intercalated fraction that is responsible for the reduced diffusion of active out of the clay, and through the polymer and, thus, to the target environment for very long periods of time.

13. Low viscosity liquid actives can be sorbed to clay carriers using Ohno's approach. When we blend heated liquid (or liquefied solid) actives, we add the active heated above its melting point (by 10° to 30°C), to the heated (same temperature) clay slowly while stirring in a mixer/blender, allowing maximum absorption within the clay, and stop mixing while the mixture is still friable (not balled or gummy, indicating excess surface absorption and crystallization).

14. In Ohno's case, his release rates are substantially higher than one would want for a long-term performance package. Applicants always talk about a friable mixture. In practice, if you go too far with active addition, then you have exceeded the clay's capacity and, thus, the mixture is non-friable (gummy), and actually results in a lot of pesticide crystallized/or gummed to the surface of the clay; thus, causing the clay particles to stick together. In practice if you go this far, you do not have what we try to teach. This friable characteristic of the clay carrier is critical to minimizing losses experienced in the 5-10 minute process of formulation into thermoplastic/thermoset products (100° to 350°C), and optimizing product release rate needs. The data for the comparison of our method of creating a loaded-friable carrier, and Ruskin's method of mixing individual components and then heating in an extruder, show that release performance is much better with our approach.

15. Our approach works effectively for creation of long term, first order releasing systems designed to perform for 10-30 years or more, for a range of actives, including bifenthrin,

trifluralin, and synthetic pyrethrins. The ideal clay loading level to maintain friability with our method is an active-ingredient loading level of 40-45% (w/w).

16. The addition of an active dissolved in a solvent (even at saturation) also causes deposition of active on the surface of the clay. The clay does load easier, but on evaporation of the solvent, much of the active ingredient diffuses out of the intercalated clays, and crystallizes on the surface of the clay. Additionally, the loading percentage is lower than our method.

17. Early studies with solvent loading of trifluralin indicated that clays could be loaded to 6% to 12% using solvent (methyl and isopropyl alcohols), and attain a fully loaded friable I.30P clay (organically modified sorption sites); this is lower than our normal 43% level using the heated active/clay method to attain a friable mixture. Use of the other noted solvents yields apparently active loading levels of 30-50%. However, these are not friable powders, and close inspection shows that the majority of the active is not intercalated. The active ingredient resides on the surface, accounting for the agglomeration of clay particles. Thus, this situation is analogous to what would be expected with Ohno's method. Additionally, solvent incorporation leads in most cases to a non-friable product that is unsuitable for extrusion or injection molding of the final thermoplastic product. Grinding, as with the Ohno method, would not resolve the problem of non-absorbed active. This surface material would represent the major controller of active release rates from the thermoplastic polymer.

18. TFN Patent Data. The following two tables compare loading levels attained with our molten TFN method with methods that use a variety of solvents. None of the solvent methods is as good as our method.

(a) Loading with molten TFN (70°C) to various heated clays. TFN added slowly (1-2 mL/min) to heated (40-60°C) and stirred clays with a whisk,using a Blakeslee mixer on low speed.

(b) Nanoclay moisture content), is <5%, with or w/o oven drying (Wt loss on drying 48 hrs at 110°C) with no effect on loading.

(c) All % loading values are TFN wt in clay/(TFN wt + clay wt).

Loading levels:	I.30P (nanoclay)	43%
	PGV (clay)	28%
	I.30E (nanoclay)	42%
	I.44P (nanoclay)	37%

(d) Solvent loading, single saturation of clay to friable mixture by stirring, w/o overloading, using nanoclay I.30P.

(e)   Drying and reloading needed to increase TFN loading onto clays, drying leads to surface crystals. This is particularly true for the toluene, xylene, ethyl acetate, and to some extent hexane. The 2 alcohols penetrate and dry more quickly, limiting surface crystals. However, loading levels for the molten TFN additions, are difficult to attain with repeated solvent additions .Reloading of solvent/TFN leads to more and more surface crystals and clay particle agglomeration.

Solvent	Max Solubility(w/w) (g TFN/1000 g)	Soln-%	Max Loading Rate (mL/15 gm Nanoclay) Loading (%)	TFN/Calculated	
Methyl Alcohol	140	13	26	12	*
Isopropyl Alcohol	65	8	25	6	*
Xylene	480	49	16	32	**
Toluene	465	46	16	31	**
Ethyl Acetate	605	61	24	51	**
Hexane	435	53	23	30	**

*   Friable, little surface crystals
**   Significant surface crystals due to evaporation of solvent and subsequent agglomeration; for any and all addition rates.

19.   All statements made herein of our own knowledge are true and all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

FURTHER DECLARANT SAYETH NAUGHT.

Date: May 13, 2009

Dominic A. Cataldo